CLAIMS

1. A method implemented by computer means to quantify, in absolute and/or relative manner, an initial population of nucleic acids in a sample of interest subjected to a succession of applications of a population amplification reaction, during which experimental measurements are taken representative of a current size of the population of at least the sample of interest,

the method comprising the following steps:

a) providing a model of the yield of the amplification reaction as a function of the succession of amplifications, said model comprising:

· a substantially constant stage for a first portion of the applications of the amplification reaction; and

· a non-constant stage for a second portion of the applications of the amplification reaction;

the first and second portions being united by a changeover region in which yield changes over between the constant and non-constant stages, said region having an amplification index corresponding substantially to the changeover;

b) using the yield model to express a relationship involving at least the changeover index and a parameter representative of the initial population size in the sample of interest;

c) determining at least the changeover index by comparison with the experimental measurements; and, in a subsequent or immediately following step d) deducing therefrom the initial population size in the sample of interest.

2. A method according to claim 1, including:

· in step b), using the yield model to express a variation that is parameterized as a function of said succession of amplifications, involving at least one parameter representing the changeover index; and

in step c), determining at least said parameter representing the changeover index by comparison with said experimental measurements.

3. A method according to claim 2, wherein said parameterized variation is representative of the current population size in the sample of interest,

wherein said variation further involves a parameter representative of the initial population size in the sample of interest; and

wherein in steps c) and d), the parameters representative of said amplification index and of the initial population size in the sample of interest are determined substantially together.

4. A method according to claim 2, wherein said parameterized variation is representative of the yield, and wherein in step c), an experimental variation of the yield is determined from said experimental measurements, in order to compare the parameterized variation with the experimental variation.

5. A method according to claim 4, including, in step d):

d1) determining a second parameterized variation that is representative of the current population size in the sample of interest, and that involves at least the parameter representing said amplification index, and a parameter representative of the initial population size in the sample of interest;

d2) applying a parameterized value for the index as determined in step c) to the second variation; and

d3) adjusting at least the parameter representative of the initial population size by direct comparison of the second variation with the experimental measurements.

6. A method according to claim 5, including:

· in step d2), applying a coarse value for the index, whereas

· in step d3), refining the value of the index while also adjusting the parameter representative of the initial population size.

7. A method according to claim 3, wherein said parameterized variation or said second parameterized variation, as the case may be:

· is representative of said experimental measurements; and

· includes a parameter corresponding to a measured value representative of the initial population size,

and wherein the measurement value of the initial population size is determined by comparing said parameterized variations with the experimental measurements.

8. A method according to claim 1, including applying a prior step of processing the experimental measurements, which step comprises subtracting a background noise from the measurements and introducing a compensation to take account of a non-zero measurement representative of the initial population size.

9. A method according to claim 7, including obtaining a measurement value for an initial population size in a standard sample having a known initial population size and deriving a proportionality relationship therebetween; and determining the value of the initial population size in the sample of interest by applying the same proportionality relationship between the initial population size and its measurement to the sample of interest.

10. A method according to claim 7, including obtaining respective measurement values for the initial population

sizes in standard samples having known initial population sizes, and by:

· establishing a dependency relationship between the initial population sizes of the standard samples and the corresponding measurement values for their respective initial population sizes; and

· after determining the measurement value for the initial population size of the sample of interest, determining the initial size of the population of interest by interpolation on said dependency relationship.

11. A method according to claim 9, including providing one or more standard samples having respective known initial population sizes, applying said succession of amplifications to said standard samples under substantially the same conditions as for the sample of interest, and determining their effective initial measurement values by comparing the parameterized variations with the experimental values.

12. A method according to claim 3, including providing a plurality of standard samples having respective known initial population sizes, applying said succession of amplifications thereto under substantially the same conditions as for the sample of interest, and determining their respective indices in application of steps a), b), and c), and by, in step d):

· establishing a dependency relationship between the initial population sizes of the standard samples and their indices; and

· after determining the index for the sample of interest, determining the initial size of the population of interest by interpolation on said dependency relationship.

13. A method according to claim 1, wherein, for a relative quantification, providing not only the population of interest, but also a reference population that is subjected to a succession of applications of the amplification reaction, the method consists in taking, respectively:

· experimental measurements representative of the size of the population of interest; and

· experimental measurements representative of the size of the reference population;

the method continuing by applying steps a), b), and c) to the reference population, with step d) consisting in determining a ratio between the respective initial sizes of the population of interest and of the reference population.

14. A method according to claim 1, including:

· expressing the experimental measurements in the form of an experimental variation of yield as a function of said succession of amplifications; and

· obtaining an experimental variation of yield as a function of said succession of amplifications comprising:

· a first region that is substantially subject to noise for low amplification index numbers; and

· followed by a second region with less noise for higher amplification index numbers.

15. A method according to claim 14, in which said non-constant stage of the yield is one of decreasing yield, the method including:

· estimating a coarse value for the constant stage of yield; and

· at least when seeking the index in said changeover region, ignoring at least some of the measurements in said less noisy second region for which the estimated yield is below a threshold value, preferably below a fraction of the constant stage.

16. A method according to claim 14, in which said non-constant stage of the yield is a stage of decreasing yield, the method including identifying said changeover region by working in the direction of decreasing amplification index number starting from said less noisy second region, and detecting a coarse amplification index at which the yield perceptibly exceeds a predetermined value (E_0=1).

17. A method according to claim 16, wherein the estimated value of said amplification index in the changeover region is refined, possibly to obtain a fractional value, by working in the direction of increasing amplification index number starting from the coarse index, by detecting an amplification index for which the yield is approximately equal to said predetermined value (E_0=1).

18. A method according to claim 1, including modeling said non-constant stage of the yield by a decreasing exponential including a decrease parameter, and determining said decrease parameter in step c) with the index in the changeover region by comparison with the experimental measurements.

19. A method according to claim 1, in which the amplification reaction is a polymerase chain reaction performed in real time.

20. A method according to claim 1, in which said measurements are measured quantities of emitted fluorescence.

21. An installation for implementing the method according to claim 1, the installation comprising:

- a sample support for supporting at least the sample of interest;

· a first apparatus for applying said succession of amplification reactions, at least to the population of interest in the sample of interest;

· a second apparatus for taking measurements representative of the current size of the population of interest; and

· computer means suitable for receiving measurement signals from the second apparatus and implementing the method according to claim 1.

22. A computer program product for storing in a memory of a processor unit or on a removable memory medium suitable for co-operating with a reader of said processor unit, the program product comprising instructions for implementing the method according to claim 1.